Original Research Article

Nutritional Status, Anthropometric and Biochemical of Down Syndrome Children with Cancer at King Abdullah Medical City Hospital in Makkah

Abstract

Background: Down syndrome children with cancer are susceptible to nutritional depletion due to the combined effects of the malignant disease and its treatment. The assessment of the nutritional status of pediatric oncology patients on admission to hospital is crucial, as nutritional status is known to influence treatment and clinical outcomes.

Objectives: This study aimed at assessing the nutritional status, life style, anthropometric and biochemical of children with cancer. The study was carried out at the at oncology department at King Abdullah medical city hospital in Makkah on 100 children having cancer and receiving treatment compared with non-cancer controls using a descriptive design, by using anthropometric parameters and prealbumine level.

Material and methods: a descriptive study on 100 Down syndrome children under 15 years with or without cancer was conducted to determine their nutritional status. The children comprised 50 patients with cancer (cases) and 50 controls seen at Down syndrome children's outpatient clinic with minor illnesses. An interview questionnaire and a physical assessment sheet collected data. Which included three parts; the first one covered the clinical examination; the second part was for anthropometric measurement and the third part was for laboratory investigations.

Result indicated that leukemia and lymphoma are the commonest cancers and chemotherapy is the therapy mostly used. Children suffer many gastrointestinal symptoms as anorexia, nausea and vomiting. The majority have abnormal anthropometric measurements, hemoglobin and serum prealbumin levels. It can be concluded that the majority of the children were suffering from anemia and malnutrition.

Conclusion: The prevalence of malnutrition in Down syndrome children with cancer is high. Arm anthropometry in conjunction with prealbumine accurately characterizing the nutritional status. Down syndrome children with cancer were significantly more malnourished than those without cancer and will require nutritional support to reduce the morbidity and mortality arising from such illness.

Key Words: *Down syndrome. Cancer. Malnutrition. Children.*

Introduction

Trisomy 21 is the commonest genetic cause of learning disability in the UK with a birth prevalence of 1 per 1000 live births (Huang et al., 1998) Adults with Down syndrome appear to age prematurely, with many showing Alzheimers-like changes in their brains in their 30s and 40s.(Kolata, 1985) Neuronal changes are evident in infants with Down syndrome. Post mortem studies have reported neuronal depletion and structural abnormalities of the brain during late gestation and early post-natal life (Becker et al., 1991) why these changes occur is not fully understood but it has been proposed that the increased activity of two enzymes, copper/zinc superoxide dismutase (SOD-1) and cystathionine-synthase, both coded for on chromosome 21, may be involved.

Increased activity of SOD-1 in children with Down syndrome 4 is thought to cause oxidative damage to neuronal cells by increasing levels of hydrogen peroxide. Evidence that oxidative stress may be involved in the premature neuronal degeneration comes from several sources. Firstly, the cerebral cortex from fetuses with Down syndrome was found to have increased activity of SOD-1 without a compensatory increase in glutathione peroxidase activity (GSH-Px).(Brooksbank and Balazs, 1984)Secondly, cortical neurons from fetuses with Down syndrome have an increased concentration of intracellular oxygen derived free radicals and increased lipid peroxidation compared to controls.(Busciglio and Yankner, 1995). Thirdly, fetal neurons in Down syndrome have increased apoptotic degeneration which appears to be prevented by the addition of antioxidants (Jovanovicet al., 1998). Finally, studies have reported increased products of lipid peroxidation in blood and urine of people with Down syndrome compared with controls (Kedziora et al .,1986),(Krishna-Murthy et al., 1986) and (Bras et al., 1989)

Evidence for a functional folate deficiency in Down syndrome is based on analytical studies in plasma and in vitro studies. The enzyme cystathionine-synthase catalyses the condensation of homocysteine with serine to form cystathionine. Increased levels of this enzyme in Down syndrome leads to significantly reduced plasma concentrations of homocysteine, methionine, S-adenosylhomocysteine and S-denosylmethionine and thereby to a “folate trap” and a functional folate deficiency(Pogribnaet al., 2001) In vitro studies have shown that adding selected nutrients (methionine, folinic acid, methyl B12, thymidine and dimethylglycine) to a cultured lymphoblastoid cell line with trisomy 21 causes a shift in one-carbon metabolism to a more normal profile.(Pogribna et al., 2001).

One study speak about the general incidence of cancer amongst individuals with Down syndrome is the same as in the general population *(Batshaw, Mark, ed.2005)*

In particular, acute lymphoblastic leukemiais at least 10 times more common in DS and the megakaryoblastic form of acute myelogenous leukemia is at least 50 times more common in DS. Transient leukemia is a form of leukemia that is rare in individuals without DS but affects up to 20 percent of newborns with DS (*Margulies, Phillip 2007).*

Nutritional status is the result of the interaction between environmental and genetic conditions in which a child lives, when these environmental conditions are favorable for life (physical, biological, nutritional and psychosocial), the genetic potential is expressed as an ideal state of nutrition, but when conditions are unfavorable such expression will be diminished, resulting in altered nutritional status, such as malnutrition, overweight and obesity, which would cause the child did not respond to a disease or its treatment suitably at a given time. (Krebs NF et al., 2011).

Malnutrition is a recognized comorbidity in cancer patients and is usually related to the type and extent of tumor. It develops mainly during the intensive phase of treatment of the disease but may be apparent at diagnosis. Therefore Nutritional support, is an important aspect of management as poor nutrition may be associated with poor prognosis. (Charles et al., 2014).
Multiple factors affecting the nutritional status in cancer patients and related to the treatment (type / dose of chemotherapy, site / dose of radiotherapy and surgery). It is also suggested that all these factors would cause an alteration in intermediary metabolism, resulting in decrease appetite, which eventually lead to lose weight, creating a vicious cycle. (Brinksma et al., 2012).

Subjects and Methods

This descriptive study on 100 Down syndrome children under 15 years with or without cancer was conducted at Oncology Department at King Abdullah Medical City Hospital in Makkah in the period from September 2016 to November 2018.

The study included 100 children below 15 years. The studied group was divided into 2 groups:

- Patient group represent 50% of studied individuals (N=50) with age ranged from (1-15) years and this group includes 26 were newly diagnosed cases with cancer and 24 were cases on chemotherapy.
- Control group: represents 50 % (N=50) apparently healthy Down syndrome children matched with the patient group for age and sex chosen from Pediatric outpatient clinic.

- **Patients inclusion criteria**:

- **Age:**Children of different cancers below 15 years admitted to oncology department.

- **Sex:** both sexes are included**.**

Children newly diagnosed with cancer**.**

- Children during intensive phase of chemotherapy with stable vital signs were included in the study.

- **Patients exclusion criteria:**

a- Presence of known metabolic or nutritional disease.

b- Presence of any other disease that may affect the child`s nutritional status as diabetes mellitus or renal failure.

c- Children with known diseases of brain; gut, liver, congenital malformation or genetic syndromes were excluded from the study.

Operational design:

1-Aquestionnaire interview: with care taking for collection of personal data, sociodemographic data and complete history taking with particular emphasis on age, sex, initial clinical presentation, associated comorbidities and nutitional history.

2-Full clinical examination:

Through physical examination were done with special consideration of anthropometric measurements:

Anthropometric measurements including:

2.1 Body weight (Wt):

Weight were calculated using SECA scale to the nearest 0.01 kg or 10 gm. The measurements were expressed in kilograms. a child should be weighed in light clothing.

2. 2 Standing height (Ht):

On astadiometer and results were expressed in centimeters.

2.3 Body mass index (BMI):

Published international age and gender specific reference values for BMI in infant and children and the task force recommended the use of BMI (calculated as weight in kilograms divided by height in meters square**)** [BMI=Weight (kg)/Height2 (m2) to indicate over nutrition or undernutrition. It accounts for the differences in body composition by defining the level of adiposity and relating it to height, thus eliminating dependence on frame size **(Hammond & Litchford., 2012**).

2.4 Mid-upper-arm Circumference (MUAC), also known as Mid-Arm Circumference (MAC) is a simple measure taken by a flexible tape placed perpendicular to the long axis of the arm, which is flexed at 90° angle. The midpoint of the upper arm half way between the acromion and the olecranon is measured and marked. Then, with the patient's arm relaxed at the side, the tape is placed around the previously marked midpoint used to define nutritional status **(Murphy et al., 2009).**

2.5 Triceps skinfold thickness *(TSF)*

TSF is measured using a skinfold caliper on the right arm at the point marked previously for the MUAC on the back of the arm. The examiner grasps the skin and subcutaneous fat tissue between thumb and forefinger above the point previously marked. After the skin, where the skinfold caliper is placed at the midpoint marked, maintaining a grasp of the skinfold. TSF is commonly adopted for research setting, but it can be also useful for identifying patient's body fat stores. **(Murphy et al., 2009).**

3-Laboratory investigations: using

-Complete blood count,

-Liver function,

-Kidney function,

- Serum albumin & Prealbumine**.**

Statistical Analysis:

Data were entered checked and analyzed using Minitab 17.0 statistical software. Quantitative data was presented as mean and standard deviation (Mean +_ SD). Comparisons between patients and controls were performed using Chi-Square test**,** Mann Whitney U test was used for non normally distributed data. Statistical significance was set at p value <0 .05 level and highly significant when p was less than 0.01.

Results:

This study was held on 100 child between ages of 1-15 years .OF those, 26 were newly diagnosed cases with cancer, 24 were cases on chemotherapy and 50 were control group. Patient group represent 50% of study individuals (N=50) while control group represents 50 % (N=50).

The male represents 56 % of study population (N=56) while female represents 54 % of study population (N= 54)

In the patient group male children were 30 child representing 60 % of the patient group while females were 20 child representing 40 % of the same group.

In the control group males were 26 child representing 52 % of control group while females were 24 representing 48 % of the same group.

Table (1): Hematological and biochemical findings among the studied patients (N=100).

Item	Studied cancer patients (N=50)	Studied Down patients (N=50)
Complete Blood picture		
WBCs		
▪ Mean ± SD	13.12 ± 4.33	5.23± 1.11
Hemoglobin		
▪ Mean ± SD	8.65 ± 1.32	11.29±1.16
Platelet count		
▪ Mean ± SD	222.8 ± 38.1	298.11±61.09
RBCs		
▪ Mean ± SD	3.21 ± 0.41	4.1±0.51
Liver function tests		
ALT		
▪ Mean ± SD	41.12 ± 8.9	33.99±7.8
AST		
▪ Mean ± SD	42.28 ± 9.1	32.67±4.9
Albumin		
▪ Mean ± SD	3.61 ± 0.49	3.51±0.23
Kidney function tests		
Urea		
▪ Mean ± SD	18.88±3.9	15.29±2.1
Creatinine		
▪ Mean ± SD	0.75±0.19	22±0.22
Serum pre albumin		
▪ Mean ± SD	112.9±15.22	201.8±33.9

Table 2: Weight changes in cancer cases

Item	Studied cancer cases (N=50)	
	No.	**%**
Weight changes within one month		
• No change	23	46
• Weight loss	26	52
• Weight gain	1	2

Table (3): Anthropometric parameters of the studied children (N=100).

Parameters	cancer cases (N=50)	Control (N=50)	P- value
Weight			
Mean ± SD	17 .17± 4.22	20.13± 3.94	0.000*
Height			
Mean ± SD	105.1 ± 12.9	115.1±9.11	0.006*
BMI			
Mean ± SD	13.8± 3.11	16.88±4.1	0.002*
MAC			
Mean ± SD	15.21 ± 3.77	18.52±3.31	0.001*
SFT			
Mean ± SD	15.07 ± 3.22	18.2±3.2	0.001*

Table (4): Proportion of malnourished children based on BMI among the studied groups

BMI	Total		Studied cancer cases (N=50)		Down Control (N=50)		Chi-square test	P-value
	No.	%	No.	%	No.	%		
Underweight <16.0	51	51.0	42	84	9	18	27.44	0.001*
Borderline 16-18.5	20	20.0	4	8	16	32		
Normal 18.5-24.5	29	16.0	4	8	25	50		

Discussion

Malnutrition in pediatric cancer is common worldwide, yet its prevalence and effects on clinical outcomes remain unclear. Cancer is the leading cause of disease-related death in children younger than the age of 14 years (**Robinson, et al., 2012).**

Cancer-related malnutrition is due to a variety of factors, including poor oral intake, abnormal metabolism of nutrients and adverse effects from chemotherapy and radiation, including nausea, vomiting, anorexia, and mucositis (**Jones, et al, 2010).**

In relating nutritional status with the type of cancer in our study, the prevalence of malnutrition was higher in patients with hematological tumors (80%) than those with solid malignancies (20%). It was observed from the study that the most common type of cancer was Leukemia, followed by Hodgkin Lymphoma then non- Hodgkin Lymphoma (Burkitt Lymphoma) then Neuroblastoma, Wilms tumors, bone tumors, and others 5 tumors so, this agreed with **Kavita Sudersanadas et al., 2017** who studied 104 of children suffering from various types of hematological malignancies and found most common type of cancer was Leukemia, followed by Lymphomas**.**

Disagreed with us **Garfólo et al., 2005** who reported that patients with solid tumors presented malnutrition more frequently compared to haematological malignancies.

In contrary, **Lemos Pdos et al., 2014** found no differences in malnutrition frequency between haematological malignancies and solid tumors.

- In our study, the complaint of weight loss appeared in cancer patients. However, in the study of **Bonaccorsi et al.,2009)** found that weight loss was used as the main criterion of nutritional assessment, with its prevalence varying between 40 and 80% during treatment.

In agreement with us **Maia-Lemos PS et al., 2016** found that average weight loss was moderate to severe in all tumor groups, except for retinoblastoma and Wilms Tumor. The difference between usual reported weight and current weight was statistically significant in patients diagnosed with carcinomas, lymphomas and bone tumors. The complaint of weight loss was given by represents 73% of the patients in this study.

But **Blum D et al., 2011** found that there is no agreement on the criteria regarding nutritional status assessment, such as the percentage weight loss that is clinically relevant**.**

Concerning the anthropometric measurements of the current study children, the results demonstrated that anthropometric parameters showed statistically significant decrease in weight, height, BMI, MAC and SFT in studied cancer patients compared with the control healthy children**.**

Maia-Lemos et al., 2016 agreed with us and found prevalence of malnutrition was higher according to TSFT and MUAC when compared with BMI, suggesting a higher sensitivity of those methods.

In agreement with our results, **Sala et al 2012** made a large study conducted in seven countries in Central America found the same to be true. When using the standard method of BMI for age the percentage of malnourished children with cancer was 45%. However, when arm anthropometry (MUAC and TSFT) was used 63% of the children were malnourished. These studies have identified the importance of using MUAC and TSFT to assess nutritional status in the pediatric oncology patient, especially in patients with intra-abdominal solid tumors**.**

Also, in agreement with our results **Brinksma et al., 2015** observed the incidence of under nutrition in newly diagnosed pediatric cancer patients to be between 23-29% using weight and height as parameters. However, it was observed that weight and height related anthropometry was still deficient in identifying patients with malnutrition. Most Patients with large tumor masses such as renal tumor or Burkitt lymphoma would not have been detected as having malnutrition if weight or height related anthropometric parameters were used alone to assess their nutritional status, as such large tumors would add to their weight. This same observation has also been documented by **Sala et al., (2012**) who noted that some intra-abdominal tumors would add up to 10-20% to patient's weight.

In our study there is significant positive correlation between weight, height, BMI, MAC, and SFT, concerning pre albumin level there is significant positive correlation between pre albumin level and RBCS, Hemoglobin and serum albumin level. In control group also there is significant strong positive correlation between weight, height, BMI, MAC, and SFT, concerning pre albumin level there is significant positive correlation between pre albumin level and BMI.

- In aggrement with our study **Frank M and Olsen SJ(2000**)found that low serum albumin, has a relation with anemia as an indicators for malnutrition. Serum albumin is an indicator for severe or late under nutrition, whereas anemia is an early indicator.

As regards the results of laboratory investigations, the present study revealed that more than one third of the studied children had anemia based on measurement of their hemoglobin level. The finding corroborates the clinical finding of a high prevalence of pallor among these children confirms that a large proportion of these children do suffer from malnutrition.

Amal Khalil et al., 2013 agreed with our data founding abnormal anthropometric measurements, hemoglobin and serum albumin levels in 105 children having cancer and receiving treatment.

Kuruğol et al.,1997. evaluated nutritional status in 45 pediatric cancer patients in several statuses of disease (diagnosis, remission, recurrence); 51.1% showed malnutrition according to the weight-for-height index, although serum albumin levels were found to be normal. When they measured prealbumin, the authors found that children in the active disease group had lower prealbumin levels than children in the remission group.

Conclusion: They concluded that only prealbumin is a reliable and sensitive indicator of mild and marginal malnutrition. They suggested that low prealbumin may be found before malnutrition is detected by anthropometric measurements.

-Yu LC et al.,1994. also reported that prealbumin is the most sensitive indicator of visceral protein status in leukemic patients. Their study involved 25 patients with leukemia, either in remission or newly diagnosed/recurrent. Fifty percent of the patients had abnormal prealbumin levels, whereas only 10–18% of the children had abnormal levels of either albumin, transferrin, or retinol-binding protein and none of the children studied had abnormal anthropometric measurements. Unlike our study, this was not a prospective study and it did not show the improvement in prealbumin values in each patient throughout chemotherapy.

- **Oguz et al.,1999** also suggested that prealbumin is the most sensitive indicator of protein energy malnutrition because it was able to indicate mild malnutrition. Anthropometric measurements were not sensitive enough to do so. Their subjects apparently were healthy children in western Nigeria, in which malnutrition is common. Others have stated that prealbumin also is a sensitive marker for the response to nutritional repletion, far more than anthropometric parameters and albumin

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